Correlation Between Filling Defect Patterns on Urography and Pathologic Staging of Ureteral Transitional Cell Carcinomas

Yi-Lun Lee, Shu-Pin Huang,[1] Min-Chen Shih,[2] Yii-Her Chou,[1] and Chun-Hsiung Huang[1]
Department of Urology, Chi-Shan Hospital, and Departments of [1]Urology and [2]Radiology, Kaohsiung Medical University Chung-Ho Memorial Hospital, Kaohsiung, Taiwan.

Although a filling defect within the ureter is the most common finding with ureteral transitional cell carcinomas (TCCs), little is known about the correlation between filling defect patterns and pathologic findings. This study was conducted to address this. Between January 1995 and January 2003, 126 pathologically confirmed TCCs of the ureter were included in our study. We classified urographic filling defects into four patterns: ovoid, polypoid, infiltrating, and plaque-like. The correlation between different filling defect patterns and pathologic findings was assessed using Pearson's Chi-squared and logistic regression methods. There were 28 (22%) ovoid filling defects, 42 (33%) polypoid filling defects, 37 (29%) infiltrating filling defects, and 19 (15%) plaque-like filling defects. Infiltrating and plaque-like filling defects were significantly associated with more advanced disease compared to ovoid and polypoid filling defects (odds ratio, 6.75; 95% confidence interval, 3.04–14.98; $p < 0.0001$). Our results suggest that filling defect presentations may signify different invasive behavior among TCCs. The distribution of ovoid, polypoid, infiltrating, and plaque-like filling defect patterns is significantly different between superficial and advanced ureteral TCCs. We suggest that classifying the filling defect patterns of ureteral TCCs may provide important preoperative information for planning treatment and predicting outcome.

Key Words: neoplasm, transitional cell carcinoma, ureter, urography
(*Kaohsiung J Med Sci* 2003;19:447–52)

Transitional cell carcinoma (TCC) of the ureter is not common worldwide, representing only 1% of all genitourinary malignancies [1–3]. However, ureteral carcinoma is relatively common in Taiwan [4–7]. Urographic examinations, including intravenous pyelography (IVP), retrograde pyelography (RP), and antegrade pyelography (AP), are important tools in detecting the tumor and defining its extent and location [1,3,8]. The most common radiographic finding in ureteral carcinoma is the presence of a filling defect within the ureter [9,10]. Although various filling defect patterns have been reported with ureteral TCCs [1,8,11], only a few studies have focused on the association between filling defect patterns and pathologic findings. Here, we report a large series of ureteral TCCs and analyze the correlation between filling defect patterns and pathologic staging.

Materials and Methods

Between January 1995 and January 2003, patients at our institution with histopathologically confirmed TCC of the ureter and with complete radiographic and histologic data

Received: January 24, 2003 Accepted: August 12, 2003
Address correspondence and reprint requests to: Dr. Yii-Her Chou, Department of Urology, Kaohsiung Medical University Chung-Ho Memorial Hospital, 100 Tzyou 1st Road, Kaohsiung 807, Taiwan.
E-mail: luinlu@ms67.url.com.tw

were eligible for inclusion in the study. Computed tomography was obtained in all cases and all patients underwent at least one urographic examination (IVP, RP, or AP). RP or AP was usually performed when IVP failed to localize the lesion or when patients had renal insufficiency.

Urographic films were reviewed by an independent radiologist (MCS) who was blinded to clinical and pathologic data. Filling defects on urography were divided into four patterns by their shape: ovoid, polypoid, infiltrating, or plaque-like [11]. We defined ovoid as a single, rounded, nodular, exophytic lesion (Figure A); polypoid as a papillary, lobulated, exophytic lesion (Figure B); infiltrating as an extensive, straggling, sessile, broad-based lesion (Figure C); and plaque-like as a thickened-wall constriction with overhanging edges and strand-like contrast filling appearance (Figure D). Surface regularity, goblet sign, stipple sign, concomitant calcification, and pseudodiverticulum were also recorded. We used the most clearly defined images from IVP, RP, and AP to categorize the patterns of the filling defects.

Pathologic staging was based on the classifications proposed by Batata et al [12]: stage A is defined as submucosal infiltration, stage B as muscular invasion, stage C as periureteral involvement, and stage D as extension to adjoining structures, regional lymph node metastases, or distant spread. Stage A was considered superficial disease because it was limited to the submucosal layer. Stages B, C, and D were considered advanced disease because invasion reached at least the muscle.

Pearson's Chi-squared and logistic regression methods were used to examine the association between various filling defect patterns and pathologic staging. Data are presented as odds ratio (OR) and 95% confidence interval (95% CI). A p value of less than 0.05 was considered statistically significant. Data analysis was performed using SPSS version 8.01 (SPSS Inc., Chicago, IL, USA).

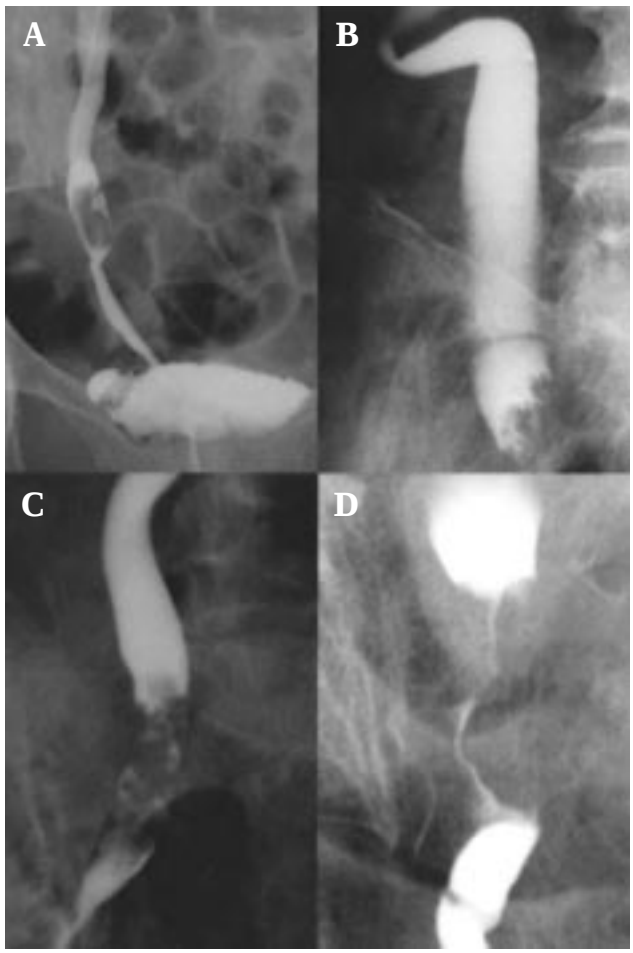

Figure. *Different filling defect patterns on urography: (A) ovoid filling defect; (B) polypoid filling defect; (C) infiltrating filling defect; (D) plaque-like filling defect.*

Results

Of 134 histopathologically confirmed cases of TCC of the ureter between January 1995 and January 2003, eight cases were excluded due to incomplete radiographic and histologic data. A total of 126 cases were enrolled in the study. Mean age at diagnosis was 66.5 years (range, 26–85). There were more male (54%) than female patients (Table 1). Most tumors were located in the upper third of the ureter; the left ureter was more frequently involved than the right ureter. There were similar numbers of superficial and advanced tumors (Table 1). Gross hematuria was the most common symptom, occurring in 70% of patients. Flank pain, urinary frequency, dysuria, lower abdominal pain, and fever were less common symptoms. Seven patients (6%) were asymptomatic and were diagnosed incidentally on ultrasonography after presentation with hydronephrosis.

Filling defect patterns were determined by RP (80 cases, 63%), AP (39 cases, 31%), and IVP (7 cases, 6%). Polypoid filling defects were most common (33.3%), followed by infiltrating (29.4%), ovoid (22.2%) and plaque-like (15.1%) filling defects (Table 2). Most lesions (81.7%) manifested with an irregular surface. The goblet sign was found in 30.2% of lesions and the stipple sign in 19.8%. Seven lesions (5.6%) showed concomitant calcification. There was no pseudodiverticulum.

The distribution of ovoid, polypoid, infiltrating, and plaque-like filling defects was significantly different between superficial disease and advanced disease (Chi-squared test,

$p < 0.0001$) (Table 3). Infiltrating and plaque-like filling defects were significantly associated with advanced disease (OR, 6.75; 95% CI, 3.04–14.98; $p < 0.0001$) (Table 4).

Table 1. Demographic and disease characteristics of 126 patients with ureteral transitional cell carcinoma

	n (%)
Male	68 (54)
Female	58 (46)
Right side	49 (39)
Left side	77 (61)
Location	
Upper third	50 (40)
Middle third	24 (19)
Lower third	49 (39)
Whole length	3 (2)
Superficial disease (Stage A)	60 (48)
Advanced disease (Stages B, C, D)	66 (52)
Stage B	26 (21)
Stage C	21 (17)
Stage D	19 (15)

Table 2. Radiographic presentation of filling defects in 126 ureteral transitional cell carcinomas

	n (%)
Shape	
Ovoid	28 (22.2)
Polypoid	42 (33.3)
Infiltrating	37 (29.4)
Plaque-like	19 (15.1)
Surface	
Regular	23 (18.3)
Irregular	103 (81.7)
Goblet sign	38 (30.2)
Stipple sign	25 (19.8)
Concomitant calcification	7 (5.6)
Pseudodiverticulum	0 (0)

Discussion

Ureteral carcinomas are mostly located in the lower third of the ureter [12–14]. In northern Taiwan, interestingly, Yang et al documented an unusually high incidence of upper urinary tract urothelial carcinoma and suggested that geographic factors or genetic predisposition might contribute to this phenomenon [4]. Our data show that the upper third of the ureter is most frequently involved in ureteral TCCs in southern Taiwan. The possible cause of this finding in southern Taiwan is undetermined. Various authors consider that the high incidence of upper urinary tract carcinomas in southern Taiwan is due to the fact that it is an area that is endemic for blackfoot disease [5–7]. Evidence suggests that the arsenic content and fluorescent substances in artesian well water are a possible etiology in blackfoot-endemic areas [15–19], but further investigation is needed to determine whether this is so. There was no significant difference in filling defect presentations among the various locations of ureteral carcinomas in our study.

IVP, RP, and AP are inexpensive and are examinations which can be easily performed to detect ureteral tumors and define their extent and location [1,3,8]. IVP is the primary initial examination for ureteral lesions, but only 6% of the tumors in our study could be clearly seen with their filling defect on IVP films. RP and AP films usually provide more satisfactory delineation of the filling defect and the precise filling defect pattern. RP and AP are more reliable than IVP and clearly revealed approximately 94% of filling defects in our study.

Both the goblet sign and stipple sign are specific features of TCC of the ureter [20,21]. However, in our study, only 30.2% of cases had the goblet sign and only 19.8% had the stipple sign. Wasserman et al reported that ureteral pseudodiverticula were frequently associated with uroepithelial malignancy [22], but we observed no

Table 3. Comparison of filling defect patterns with tumor stage

Filling defect pattern	N	Tumor stage	
		Superficial disease (A) *n* (%)	Advanced disease (B, C, D) *n* (%)
Ovoid	28	20 (71)	8 (29)
Polypoid	42	27 (64)	15 (36)
Infiltrating	37	9 (24)	28 (76)
Plaque-like	19	4 (21)	15 (79)

Chi-squared test, $p < 0.0001$.

Table 4. Correlation between filling defect patterns and tumor stage in ureteral transitional cell carcinomas

Filling defect pattern	Superficial disease *n* (%)	Advanced disease *n* (%)	OR (95% CI)
Ovoid or polypoid	47 (67)	23 (33)	1.00
Infiltrating or plaque-like	13 (23)	43 (77)	6.75 (3.04–14.98)

OR = odds ratio; CI = confidence interval. Logistic regression test, $p < 0.0001$.

pseudodiverticulum in our study. The role of these specific signs may need to be further elucidated.

The distribution of the four filling defect patterns was statistically different between superficial and advanced ureteral TCCs ($p < 0.0001$) (Table 3). Infiltrating and plaque-like filling defects were significantly associated with advanced TCCs, while ovoid and polypoid filling defects were associated with superficial TCCs (OR, 6.75; 95% CI, 3.04–14.98; $p < 0.0001$) (Table 4). These findings are compatible with the view that grossly polypoid and pedunculated urothelial tumors are less invasive than sessile or flat lesions [1]. Our results demonstrated that ureteral TCCs have different invasive behavior and can be identified through various filling defect patterns seen on urographic films.

Total nephroureterectomy with excision of the bladder cuff is the standard therapy for ureteral malignancy [2,13, 14]. However, some authors advocate nephron sparing surgery (NSS), including segmental ureteral resection or transureteral endoscopic management in selected patients [23–26]. These methods are controversial due to observed recurrence rates of 12% to 50% [23–28]. To our knowledge, no study has made recommendations on how to preoperatively select patients for NSS for ureteral carcinomas. Based on our urographic and pathologic findings, we postulate that an aggressive treatment strategy is needed for infiltrating and plaque-like filling defects due to the possibility of invasive tumor behavior, whereas NSS may be appropriate for less invasive ureteral TCCs with ovoid and polypoid filling defects.

Our study has some limitations due to its retrospective design. We attempted to reduce observer bias by blinding one independent radiologist to the clinical and pathologic data; the influence of observer bias should be minimal. A large-scale, prospective clinical trial is warranted to further validate our findings.

In conclusion, infiltrating and plaque-like filling defect patterns are significantly associated with advanced TCCs of the ureter, while ovoid and polypoid filling defect patterns are associated with superficial TCCs of the ureter. The filling defect pattern on urography may provide important preoperative information to aid treatment planning and deserves further investigation to validate its application in clinical management.

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